

## ORIGINAL RESEARCH

### **Prognostic Factors Associated with Mortality in Covid 19 Disease: A Retrospective Single Centre Institutional Study**

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#### **ABSTRACT**

**Background:** To evaluate the association of the demographic, clinical sign and symptoms and laboratory biomarkers in predicting the mortality in COVID-19 infected patients.

**Materials and Methods:** This was a single centre retrospective observational study carried out in a tertiary care centre of a tribal region of central India, which was a referral centre for COVID-19. Parameters taken into account were physiological parameters, symptoms at admission, radiographic findings and laboratory findings.

**Results:** Out of 103 deaths included in this study 76 were male and 37 females (2:1). Mean age of the deceased were 54.90 years (18-90 years). The most common symptom on admission was breathlessness in 92 patients (89.32%). Abdominal symptoms like diarrhoea and vomiting were associated in 7.7 % of the deceased patients only. Most of the patients who died were older patients having age 60 years and above (65.04 %). Most of the patients who died had Spo<sub>2</sub> less than 90 % on admission (85.43 %). Lymphopenia (92.23 %) was the most commonly observed finding on blood investigations done in deceased patients followed by increased CRP level (78.64 %). Comorbidities were present in 77 patients out of 103 patients (74.75%) included in this study. Diabetes and hypertension were being the most common comorbidities associated in these patients. Death was not commonly observed in patients with COVID 19 associated with respiratory diseases.

**Conclusion:** Identified prognostic factors can help clinicians and policy makers in tailoring management strategies for patients with COVID-19 infectious disease while researchers can utilize our findings to develop multivariable prognostic models that could eventually facilitate decision-making and improve patient important outcomes.

**Keywords:** COVID-19, Global pandemic, Prognostic Factors, Mortality.

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## INTRODUCTION

COVID-19 was declared as a global pandemic by WHO on 11 March 2020.<sup>[1]</sup> It has now spread to over 200 countries and territories worldwide. With the cumulative cases in the world approaching 34 million and cumulative deaths touching more than 500 million, while the total cases in India is increasing rapidly to more than 40 million with total mortality till now is about more than 5 lac.<sup>[1,2]</sup>

COVID 19 pandemic was a big challenge for the health system especially in India where the population at risk was very high and the hospitals and health personals were very limited which might lead to overburden and affect the outcome of the patients suffering from COVID 19. It was difficult to categorize the patients with COVID-19 infection on the basis of their presentation initially as most of the patients were either asymptomatic or presented with milder symptoms like fever, dry cough, myalgia, sore throat, headache and non-respiratory symptoms and then rapidly developed shortness of breath, altered sensorium, signs of hypoxemia and at last MODS.<sup>[3-7]</sup>

Identifying the predictors of COVID-19 disease severity along with risk categorization of them will improve the management and outcome specially in term of decreased morbidity and mortality. The demographic, clinical sign and laboratory parameters are easily available and can be used for the assessment for the predictors of mortality in COVID 19 patients. It has been shown in various studies that laboratory markers especially lymphopenia, decreased platelet count, elevated liver function values and inflammatory markers were associated with poor outcome. In majority of the studies, patients had co-existing co-morbidities with most common being hypertension, diabetes and cardiovascular disease. These are high risk patients and early identification of such high-risk patients will help in better utilization of health care resources for more severe COVID-19 patients.<sup>[8-11]</sup>

Clinical observations, patient's demographics data and blood investigations at hospital admission had been used for determining the risk of mortality in COVID 19 patients. The corona virus clinical characterisation consortium mortality score had been developed using eight parameters and classified patients in the low, intermediate, high or very high likelihood of death on the basis of a total score from 0 to 21, with higher number reflecting greater risk. The parameters included in this score are age, sex, number of comorbidities, peripheral oxygen saturation, Glasgow coma scale score, urea level and C reactive protein concentration.<sup>[12,13]</sup>

### Aim

The aim of this study was to evaluate the association of the demographic, clinical sign and symptoms and laboratory biomarkers in predicting the mortality in COVID-19 infected patients.

## MATERIALS & METHODS

**Study design and participants:** This was a retrospective single-centre study at Government medical college and allied hospitals, Ratlam, M.P. India, a tribal dominated area of central India. All patients who were admitted at Government medical college and allied hospital, Ratlam and diagnosed as having COVID 19 disease confirmed by laboratory investigations as per ministry of health and family welfare guidelines and died during their treatment course in this hospital from June 2020 to December 2020 were enrolled in this study.

### Inclusion criteria

- All patients who were admitted at Government medical college and allied hospital, Ratlam, M.P. and diagnosed as having COVID 19 disease confirmed by laboratory investigations as per ministry of health and family welfare guidelines and died during their treatment course in this hospital from June 2020 to December 2020.

### Exclusion criteria

- Patients who were brought dead or died after discharge in other hospitals were excluded.
- Patients who were treated elsewhere and data was not available were excluded.

Procedures: We collected demographic, clinical, laboratory and management data of the COVID 19 deceased patients from patient's medical records and death audit reports. Direct communication with the in-charge consultant or attending doctors and other healthcare workers were done if any data was missing from the records or any clarification was needed.

We included in the analysis the following:

- Physiological parameters: age, sex, temperature, heart rate, respiratory rate, blood pressure, Glasgow Coma Scale score, oxygen supplementation and peripheral oxygen saturation (SpO<sub>2</sub>).
- Symptoms at admission: fever (core temperature >37.5°C), dyspnoea, cough, fatigue or other (including sore throat, headache, diarrhoea, abdominal pain).
- Radiographic findings: based on chest X-ray or HRCT Chest, patients were categorized as normal, monolateral ground-glass opacity or interstitial involvement and bilateral pneumonia.
- Laboratory findings: hemoglobin, total white cell blood count, serum creatinine, blood urea nitrogen, alanine aminotransferase, lactate dehydrogenase, prothrombin time, D-dimer, ferritin and C-reactive protein (CRP).
- Clinical history: coronary artery disease or congestive heart failure, hypertension, diabetes, chronic obstructive pulmonary disease, myasthenia Gravis, pulmonary tuberculosis, renal failure, CVA, hypothyroidism, malignancy, asthma, arthritis and morbid obesity.

Outcomes: We had analysed demographics characteristics, signs and symptoms on admission, associated co-morbidity, laboratory results, chest radiography and CT findings if done to COVID 19 deceased patients.

## RESULTS

**Table 1: Symptoms Associated with Covid 19 Deceased Cases**

Symptoms	Numbers
Fever	65 (63.10 %)
Cough	48 (46.60 %)
Breathlessness	92 (89.32 %)
Diarrhoea	2 (1.9 %)
Vomiting	6 (5.8 %)
Weakness	5 (4.8 %)
Bodyache	11 (10.67 %)
Altered Sensorium	1 (0.9 %)

**Table 2: Clinical and radiological parameters at the time of admission in covid 19 deceased patients.**

		Total deaths
Spo <sub>2</sub> on Admission	94 -100	10
	93-91	5
	less than 90	88
Respiratory Rate	20- 24	58
	25-30	45

CT Score	Upto8	30
	9-18	38
	19 – 25	12
Co-morbidities	Nil	26
	1	26
	2	29
	3	16
	4	3
Duration of symptoms	1-3 Days	22
	4-7 Days	54
	1-2 weeks	20
	Morethan 2 weeks	8
Age	Upto40	3
	40-60	33
	60 and above	67

**Table 3: Laboratory Parameters in COVID 19 Deceased Patients**

Laboratory parameters	Number
Deranged Creatinine	31 (30.09 %)
Deranged Blood Sugar Level	62 (60.19 %)
Increased WBC Count	36 (34.95 %)
Increased CRP	81 (78.64 %)
Lymphopenia	95 (92.23 %)
D-Dimer	62 (60.19 %)

**Table 4: Co-Morbidities Associated in COVID 19 Deceased Patients**

Co-morbidities	Total deaths
Diabetes Mellitus	48 (46.60 %)
HT	48 (46.60 %)
Renal Failure	10 (9.7 %)
CAD	17 (16.50 %)
COPD	3 2.9 %
CVA	4 (0.38)
Hypothyroidism	2 (0.19 %)
Pulmonary Tuberculosis	1 (0.09 %)
Asthma	6 (5.8 %)
Arthritis	1 (0.09 %)
Myasthenia Gravis	2 (0.19 %)
Carcinoma Prostate	1 (0.09 %)
Morbid Obesity	1 (0.09%)
Nil	26 (25.24 %)

Out of 103 deaths included in this study 76 were male and 37 females (2:1). Mean age of the deceased were 54.90 years (18-90 years). The most common symptoms on admission was breathlessness in 92 patients (89.32%) followed by fever in 65 patients(63.10%) and cough in 48 patients (46.60%). Out of 103 patients, 39(37.86%) had both fever and cough and 35(33.98%) had fever, cough and breathlessness at the time of admission. Abdominal

symptoms like diarrhoea and vomiting were associated in 7.7 % of the deceased patients only. [Table1].

Most of the patients who died were older patients having age 60 years and above (65.04 %) and least in younger age group less than 40 (0.29%). Most of the patients who died had Spo2 less than 90 % on admission (85.43 %) while 10 patients had Spo2 94 and above (0.97%). CT Score or HRCT Thorax was available in 80 patients (77.66%). Out of which CT score was up to 8 in 30 patients (37.5%), 9-18 in 38 patients (47.5%) and 19-25 in 12 patients (15 %). Out of 88 patients with Spo2 less than 90, HRCT thorax report was available in 68 patients. 32 patients (47.05 %) had CT Score 9-18 on initial HRCT Thorax while 25 had score less than 9(36.76 %) and 19-25 in 11 patients (16.17%). [Table2] Out of 68 patients who were categorized as severe illness category as per clinical signs and guidelines for management of COVID 19, only 16.17 % were fall under severe lung infections as per CT Score criteria on HRCT thorax.

Lymphopenia (92.23 %) was the most commonly observed finding on blood investigations done in diseased patients followed by increased CRP level (78.64 %). Altered blood sugar level and increased D – Dimer was present in 60.19 % of the patients included in this study. [Table3]

Co-morbidities were present in 77 patients out of 103 patients (74.75%) included in this study. Diabetes and hypertension were being the most common comorbidities associated in these patients (46.60%), followed by coronary heart disease (16.50%) and renal failure (9.7%). Respiratory diseases like asthma were present in 6 (5.8 %), COPD in 3 (2.9%) and pulmonary tuberculosis in 1 patient only (0.97%). Death was not commonly observed in patients with COVID 19 associated with respiratory diseases. [Table4]

### **Statistical analysis:**

After getting the required information, the collected data were coded, tabulated and analysed. The various statistical techniques i.e. the mean, standard deviation and test of significance (t-test and chi-square test) were used for drawing valid conclusions. Statistical analysis was done using the student t-test. SPSS 13.0 software was used to calculate a p-value.  $P < 0.05$  was taken as statistically significant. A descriptive analysis was done on all variables to obtain a frequency distribution. The mean + SD and ranges were calculated for quantitative variables. Continuous variables were compared by the Student t-test. Proportions were analyzed with the chi square test.

### **DISCUSSION**

Garcia PD et al gave initial report of the European RISC-19-ICU prospective observational cohort. Similar to our study, they gave prognostic factors associated with mortality risk and disease progression in critically ill patients. Risk Stratification in COVID-19 patients in the Intensive Care Units was created to provide near real-time assessment of patients developing critical illness due to COVID-19. The European RISC-19-ICU cohort demonstrates a moderate mortality of 24% in critically ill patients with COVID-19. Despite high ARDS severity, mechanical ventilation incidence was low and associated with more rescue therapies. The main mortality predictors in these critically ill patients were markers of oxygenation deficit, renal and microvascular dysfunction, and coagulatory activation. Elevated risk of bloodstream infections underscores the need to exercise caution with off-label therapies.<sup>[13]</sup>

Covino M et al studied clinical characteristics and prognostic factors in COVID- 19 patients aged  $\geq 80$  years. This was a single-centre, retrospective, observational study carried out in a referral centre for COVID-19 in central Italy. They reviewed the clinical records of patients and identified risk factors for death, by a uni and multivariate Cox regression analysis. The

present data suggest that risk of death could be not age dependent in patients aged  $\geq 80$  years, whereas severe dementia emerged is a relevant risk factor in this population. Severe COVID-19, as expressed by elevated lactate dehydrogenase and low oxygen saturation at emergency department admission, is associated with a rapid progression to death in these patients.<sup>[14]</sup>

The objective of systematic review by Izcovich A et al was to identify prognostic factors that may be used in decision-making related to the care of patients infected with COVID-19. They included studies that assessed patients with confirmed or suspected SARS-CoV-2 infectious disease and examined one or more prognostic factors for mortality or disease severity. They studied 207 studies and found high or moderate certainty that the following 49 variables provide valuable prognostic information on mortality and/or severe disease in patients with COVID-19 infectious disease: demographic factors, patient history factors, physical examination factors, laboratory factors, radiological factors and high SOFA score (sequential organ failure assessment score).<sup>[15]</sup>

Sisó-Almirall A did a case series from Barcelona on prognostic factors in Spanish COVID-19 patients. It was a descriptive, observational, retrospective study in three primary healthcare centres with an assigned population of 100,000. They concluded that determining the clinical, biological and radiological characteristics of patients with suspected COVID-19 infection will be key to early treatment and isolation and the tracing of contacts.<sup>[16]</sup>

Prognostic factors study for adverse outcomes in COVID-19 infection was done by Udwadia ZF et al. Similar study was done by Mostaza JM et al on clinical course and prognostic factors of COVID-19 infection in an elderly hospitalized population. Older subjects had a higher risk of COVID-19 infection and a greater mortality. Elderly patients with COVID-19 infection have a similar clinical course to younger individuals. Previous treatment with RAAS inhibitors and demographic, clinical and laboratory data influence prognosis.<sup>[17,18]</sup>

COVID-19 has become one of the worst infectious disease outbreaks of recent times, with over 2.1 million cases and 120,000 deaths so far. Sun Y, Dong Y et al studied characteristics and prognostic factors of disease severity in patients with COVID-19. Their study investigated the demographic, clinical, laboratory and imaging features of 63 patients with COVID-19 in Beijing. Thirty percent of patients had severe or critically ill disease. Fever was the most common presentation (84.1). They found that lymphocyte and eosinophils count were significantly decreased in patients with severe disease. Eosinopenia was a feature of higher levels of severity of the infection. Peripheral CD4+, CD8+ T lymphocytes, and B lymphocytes were significantly decreased in severe and critically ill patients. The inflammatory markers CRP, ESR and ferritin were elevated in patients with severe disease or worse. IL-6 levels were also higher, indicating that the presence of a hyperimmune inflammatory state. C-reactive protein level, CD8 T lymphocyte counts and D-dimer were independent predictors of the disease severity.<sup>[19]</sup>

Pérez FM et al described a retrospective cohort study clinical features, co-morbidity and prognostic factors associated with in-hospital mortality in a cohort of COVID-19 admitted to a hospital. A descriptive study and an analysis of the factors associated with intrahospital mortality were performed. In a multi-variant analysis, the variables significantly associated to mortality were the presence of cardiopathy (CI 95% OR 2,58–67,07), levels of LDH  $\geq 345$  IU/L (CI 95% OR 1,52–46,00) and age  $\geq 65$  years (CI 95% OR 1,23–44,62). The presence of cardiopathy, levels of LDH  $\geq 345$  IU/L and age  $\geq 65$  years are associated with a higher risk of death during hospital stay for COVID-19. This model should be validated in prospective cohorts.<sup>[20]</sup>

## CONCLUSION

Identified prognostic factors can help clinicians and policy makers in tailoring management strategies for patients with COVID-19 infectious disease while researchers can utilize our

findings to develop multivariable prognostic models that could eventually facilitate decision-making and improve patient important outcomes.

### **Declarations:**

Funding: None Conflicts of interest/Competing interests: None Availability of data and material: DCH and DCHC, Government Medical College Ratlam Code availability: Not applicable Ethical Consideration: There are no ethical conflicts related to this study. Consent for publication: Consent taken

### **What This Study add to Existing Knowledge**

Coronavirus disease 2019 (COVID-19) is associated with a high disease burden with 10% of confirmed cases progressing towards critical illness. Nevertheless, the disease course and predictors of mortality in critically ill patients are poorly understood. Determining the clinical, biological and radiological characteristics of patients with suspected COVID-19 infection will be key to early treatment and isolation and the tracing of contacts. Elderly patients with COVID-19 infection have a similar clinical course to younger individuals. Previous treatment with RAAS inhibitors, and demographic, clinical and laboratory data influence prognosis.

### **Contribution by Different Authors**

First Author: Dr Atul Kumar. Associate Professor, Department of Surgery, Government Medical College, Ratlam. Study design, Concept, Data Collection and Statistical Analysis

Second Author: Dr Devendra Nargawe. Assistant Professor, Department of Pediatrics, Government Medical College, Ratlam. Data Collection, References and Discussion

Third Author Dr. Sanjay Kumar Dubey. Associate Professor, Department of Medicine, Government Medical College, Ratlam. Data collection, Statistical Analysis and interpretation of data

Fourth And Corresponding Author - Dr. Shivani Sinha. Demonstrator, Department of Microbiology Government Medical College, Ratlam. Concept, Manuscript preparation and drafting the paper

Fifth Author Dr. Neelam R. Charles. Professor and HOD, Department of Surgery, Government Medical College, Ratlam. Guidance and final approval of the paper

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